

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
22 March 2001 (22.03.2001)

PCT

(10) International Publication Number
WO 01/19844 A1(51) International Patent Classification⁷: C07H 21/04,
C07K 14/435, 14/705, C12N 5/10, 15/00, 15/12, G01N
33/53[US/US]; Apt. 3D, 17 East 89th Street, New York, NY
10128 (US). LI, Yixin [US/US]; Apt. 9H, 430 East 63rd
Street, New York, NY 10021 (US).

(21) International Application Number: PCT/US00/24966

(74) Agents: ZITRON, Anne, E. et al.; Darby & Darby P.C.,
805 Third Avenue, New York, NY 10022-7513 (US).(22) International Filing Date:
13 September 2000 (13.09.2000)(81) Designated States (*national*): CA, JP, MG, US.

(25) Filing Language: English

(84) Designated States (*regional*): European patent (AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,
NL, PT, SE).

(26) Publication Language: English

(30) Priority Data:
60/153,625 13 September 1999 (13.09.1999) US**Published:**(71) Applicant (*for all designated States except US*): NEW
YORK SOCIETY FOR THE RELIEF OF THE RUP-
TURED AND CRIPPLED, MAINTAINING THE
HOSPITAL FOR SPECIAL SURGERY [US/US]; 535
East 70th Street, New York, NY 10021 (US).

— With international search report.

— Before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments.

(72) Inventors; and

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*(75) Inventors/Applicants (*for US only*): CROW, Mary, K.

WO 01/19844 A1

(54) Title: ALTERED NUCLEOTIDE SEQUENCE IN CD40 LIGAND PROMOTOR

(57) **Abstract:** This invention relates to alterations in the CD40 ligand (CD40L) promoter, and methods of identifying individuals at risk for a disease or condition in which an elevated expression of CD40L is a factor. Such diseases include autoimmune diseases such as Rheumatoid Arthritis (RA). Nucleic acids encoding for the altered CD40L promoter are provided. These nucleic acids provide diagnostic and therapeutic tools for evaluating and treating or preventing diseases or conditions in which an elevated expression of CD40L is a factor. The invention provides a diagnostic method in which a blood or tissue sample is taken from an individual at risk for RA, nucleic acid is extracted, and the CD40L promoter sequenced. The invention also provides a diagnostic method in which a blood or tissue sample containing cells expressing CD40L is taken from an individual at risk for RA, the transcriptional activity of the CD40L gene is measured, and compared to a control value. The invention further relates to screening for compounds that modulate the activity of an altered CD40L promoter. Such compounds can be used in treating or preventing diseases in which elevated expression of CD40L is a factor.